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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/964,042	WEICHSELBAUM ET AL.	
	Examiner	Art Unit	
	J. E. ANGELL	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,10,12,13 and 16-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,10,12 and 16-23* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 9/14/2009.

The amendment filed 9/14/2009 is acknowledged and has been entered.

Claims 1, 3-5, 10, 12, 13, 16-23 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

MPEP § 706.03(o) indicates:

> *In amended cases, subject matter not disclosed in the original application is sometimes added and a claim directed thereto. Such a claim is rejected on the ground that it recites elements without support in the original disclosure under 35 U.S.C. 112, first paragraph,*

Waldemar Link, GmbH & Co. v. Osteonics Corp. 32 F.3d 556, 559, 31 USPQ2d 1855, 1857 (Fed. Cir. 1994); In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed... If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure. (Emphasis added).

Claims 22 and 23 encompass a method for treating a patient with a radiation-resistant cancer by administering a therapeutically effective amount of a HSV comprising a modified genome such that it is rendered incapable of expressing an active gene product from only one copy of each of ICP0, ICP4, ORFO, ORFP and γ1 34.5 and further comprising a U_L24 and U_L56 gene each rendered incapable of expressing an active gene product. The claims encompass treating any type of cancer that is radiation-resistant and using any HSV that comprises a the indicated modification. Looking to the specification for support, there does not appear to be support for the entire scope encompassed by the instant claims.

It is also noted that page 10, lines 25-29 discloses:

> These results demonstrate for the first time dramatic antitumor efficacy of R7020 in the treatment of experimental human tumors frequently resistant to common cancer treatments and suggest that, while R7020 is an effective antitumor agent by itself, combining irradiation with R7020 also provides more rapid and complete tumor cell destruction.

Based on the above cited disclosure, the specification only appears to provide support for treating radiation resistant epidermal carcinoma cells using R7020. It is noted that SQ-206 cells are radiation-resistant epidermal carcinoma cells (as indicated on page 7, lines 1-3), which is considered to provide support for radiation resistant epidermal carcinoma cells, but not for the entire genus of all radiation resistant cancers.

Should applicants traverse, they are asked to provide the exact page and line numbers where support can be found.

3. Claims 1, 3-5, 10, 12, 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods when the HSV is limited to R7020 (all claims) and when the radiation-resistant cancer (claims 22-23) is limited to radiation-resistant epidermal cancer, does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The nature of the invention is a therapeutic method for treating cancer using a mutant HSV. Thus, the invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

First, the claims are broad with respect to the genus of HSVs that can be used in the claimed methods. Specifically, in their broadest embodiments, the claims encompass the use of any HSV comprising a modified genome such that it is rendered incapable of expressing an active gene product from only one copy of each of ICP0, ICP4, ORFO, ORFP and γ1 34.5 and further comprising a U_L24 and U_L56 gene each rendered incapable of expressing an active gene product. It is noted that, given the broadest reasonable interpretation of the claims, the claims encompass any HSV having the indicated modifications as well as any other possible deletion or substitution of the HSV genome. It is also noted that claims 3-5, 10, 12 identifies a number of

specific modifications that the HSV can be required to have. Therefore, the claims encompass using a large number of different HSVs.

Second, claims 22 and 23 are also broad in the sense that they encompass treating any type of radiation-resistant cancer.

The state of the prior art and the unpredictability of the claimed invention

The prior art of record does not teach reducing mass of a non-central nervous system tumor using any HSV that has the claimed modifications wherein the HSV is safe for administration to a patient. Nor does the prior art teach treating radiation-resistant cancer using said HSV. As indicated above, the claims are very broad with respect to number of different HSVs encompassed by the claims as well as the types of radiation-resistant cancers encompassed by claims 22 and 23. Therefore, the claims encompass using any of a myriad of different HSVs for treating a myriad of different radiation-resistant cancer types; however, the prior art provides little or no guidance for using the any of the claimed HSVs for treating cancer. Thus, there is a relatively incomplete understanding of the field of the broadly claimed invention.

In *In re Vaeck,* 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), the Court ruled that a rejection under 35 U.S.C. 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims.

Working Examples and Guidance in the Specification

The specification only discloses that R7020 HSV was effective for treating radiation-resistant epidermal cells, as well as prostate adenocarcinoma cells and hepatoma adenocarcinoma

cells. That is, the specification only describes treating **one** type of radiation-resistant cancer: radiation-resistant epidermal carcinoma cells.

Quantity of Experimentation

Considering the breadth of the claims with respect to the number of different HSVs encompassed by all the rejected claims as well as the different types of radiation-resistant cancers encompassed by claims 22-23, additional experimentation would be required in order to practice the full scope encompassed by these claims. The amount of additional experimentation would be enormous considering and would amount to trial-and-error experimentation to determine which HSV encompassed by the claims would be effective in the claimed methods and which ones would not, and to determine which radiation-resistant tumors could be effectively treated with the HSVs. Furthermore, considering the relatively incomplete understanding of field, the elucidation of the HSVs which would be effective in the claimed methods would amount to a significant advancement in the state of the art.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the limited amount of working examples and guidance provided, and the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure for the instant claims. Therefore, additional experimentation is required before one of skill in the art could make and

use the claimed invention. The amount of additional experimentation required to perform the broadly claimed invention is undue.

Response to Arguments

4. Applicant's arguments filed 9/14/2009 have been fully considered but they are not persuasive.

5. With respect to the new matter rejection, Applicants argue that the Examiner has not met his burden of establishing a *prima facie* case for the rejection.

6. In response, the claims have been amended from their original submission and are broader than that which is described in the specification. As indicated in the rejection,

MPEP §2163.02 indicates:

> *Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed... If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.*

7. Since the claims are broader than what is described in the specification, the claim now defines an invention that was NOT clearly conveyed to those skilled in the art at the time the application was filed. Furthermore, the claims have been amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed. Therefore, per MPEP §2163.02, the examiner should conclude that the claimed subject matter is not described in that

application. Thus, at least for this reason, the Examiner has met his burden of establishing a *prima facie* case for the rejection.

8. Applicants refer to page 10, lines 25-29 of the specification and argue that nothing in the passage limits the invention to SQ-206 cells and the passage also broadly describes treatment of tumors that are resistant to common cancer treatment.

9. In response, it is respectfully pointed out that the rejection is based on the fact that claims 22-23 are now drawn treating any type of radiation-resistant cancer, while the specification only discloses treating one type of radiation-resistant cancer: radiation-resistant epidermal cancer cells. It is acknowledged that the specification discloses treating SQ-206 cells (a type of radiation-resistant epidermal cancer cell), and this disclosure is sufficient to support treating radiation-resistant epidermal cells, but not sufficient to support treating all radiation-resistant tumor cells. In other words, the Examiner is not indicating that the claims should be limited to SQ-206 cells. The Examiner is only indicating that the claims should be limited to radiation-resistant epidermal cells. Furthermore, none of the passages referred to by the Applicants supports treatment using any HSV other than HSV-7020.

10. Applicants point out that 37 CFR 1.118 is currently reserved and that the proper rule should be 1.121(f). Applicants assert that 1.121(f) is directed to amendments to the disclosure, not the claims.

In response, the Examiner appreciates the Applicants' identification of the proper rule number. Furthermore, the claims are part of the disclosure of the invention, thus the argument that it should not apply to the amendment to the claims is not persuasive. Additionally, it is noted that MPEP § 706.03(o) indicates:

> *In amended cases, subject matter not disclosed in the original application is sometimes added and a claim directed thereto. Such a claim is rejected on the ground that it recites elements without support in the original disclosure under 35 U.S.C. 112, first paragraph, Waldemar Link, GmbH & Co. v. Osteonics Corp. 32 F.3d 556, 559, 31 USPQ2d 1855, 1857 (Fed. Cir. 1994); In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981). See MPEP § 2163.06 - § 2163.07(b) for a discussion of the relationship of new matter to 35 U.S.C. 112, first paragraph. New matter includes not only the addition of wholly unsupported subject matter, but may also include adding specific percentages or compounds after a broader original disclosure, or even the omission of a step from a method. See MPEP § 608.04 to § 608.04(c)…*

Furthermore, MPEP §2163.06 specifically indicates:

> *If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).*

Applicants argue that post filing art (Exhibits A-G) confirm that the application, as filed, provides enabling support for the full scope of the pending claims.

In response, Applicant is reminded that MPEP § 2164.01 indicates that the application, when filed, must contain sufficient information to enable one of skill in the art how to make and use the claimed invention. In other words, the claims must be enabled at the time of filing. Furthermore, Exhibits A-G are drawn to HSV vectors which are not specifically disclosed in the instant application. For instance, Applicants indicate that NV1020 is a derivative of R7020; however, the application as filed, does not specifically disclose NV1020. It is acknowledged that the specification may broadly disclose a genus of HSVs that may include NV1020, but the disclosure does not clearly convey to those skilled in the art that applicants had possession of NV1020. Therefore, Applicants arguments are not persuasive.

Applicants argue that: (1) the nature of the invention does not render the claims non-enabled, (2) the claims are not overbroad, (3) that the state of the prior art coupled with the

examples and guidance provided by the application are sufficient to enable the claimed invention, (4) the amount of additional experimentation required to make and use the broadly claimed invention to its full scope is not undue. In response, Applicants argue each element of the Wands analysis separately, but it the consideration of the Wands factors, as a whole, that renders the claims non-enabled to their full scope. That is considering the nature of the invention, the breadth of the claims, the state of the prior art, the working examples and guidance provided by the application, AND the amount of additional experimentation required, it has been determined that the disclosure does not provide an enabling disclosure for the full scope encompassed by the claims. Each element of the Wands factors was addressed in the rejection, and all elements of the Wands factors were considered in determining if the disclosure enabled the full scope encompassed by the claims. It is noted that limiting claims 1, 3-5, 10, 12, 16-21 to HSV R7020 would obviate the rejection of those claims and limiting claims 22-23 to HSV R7020 and radiation-resistant epidermal cancer cells would obviate the rejection as it pertains to those claims.

Allowable Subject Matter

11. Claim 13 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. ANGELL whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 7:00 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. ANGELL/
Primary Examiner, Art Unit 1635